

Gubra ob/ob-NASH model

The accelerated biopsy-confirmed ob/ob-NASH mouse model with progressive fibrosis.

Gubra ob/ob diet-induced and biopsy-confirmed mouse model of NASH with progressive hepatic fibrosis

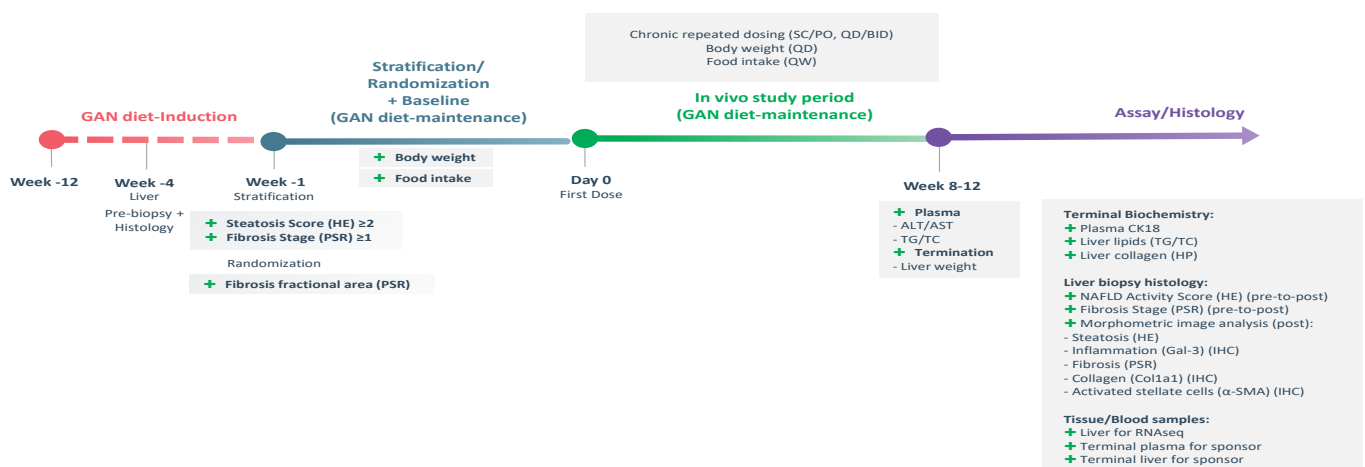
The Gubra ob/ob-NASH mouse model exhibits key hallmarks of metabolic-associated NASH with progressive liver fibrotic development, uniquely identified by baseline liver biopsy and objectively assessed by individual histopathological pre-to-post changes evaluated by clinical-derived NAFLD Activity Score and Fibrosis Stage.

Key model traits

- GAN diet high in fat, fructose and cholesterol for 12 weeks before study start
- Genetically-induced obesity and metabolic disease
- Accelerated onset of biopsy-confirmed steatosis and fibrosis
- Rapid progression to bridging fibrosis (stage F3)
- Clinical histopathological endpoints (pre-to-post)
- Prophylactic and therapeutic evaluation of drug efficacy

Diet	40 % fat (palm oil) 40% carbohydrates (20% fructose) 2% cholesterol	Gubra Amylin NASH (GAN) diet. Hallmarks of NASH and moderate hepatic fibrosis developed after 12 weeks on diet.
Strain	Male B6.V-Lepob/JRj mice	

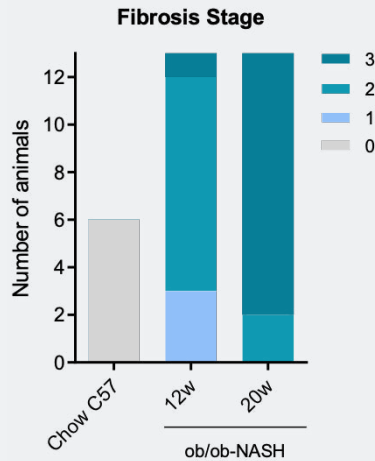
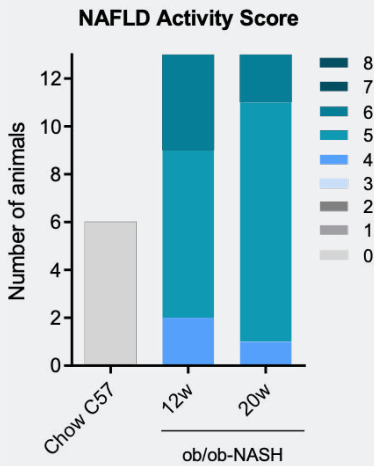
Study outline



Metabolic and biochemical characteristics

ob/ob-NASH mice develop severe obesity-driven hyperinsulinemia and hepatomegaly with pronounced steatosis and elevated biomarkers of cell injury and fibrosis.

	CHOW C57	ob/ob-NASH
Body weight (g)	28.3 ± 0.8	69 ± 1
Liver weight (g)	1.3 ± 0.1	6.9 ± 0.3
Plasma insulin (pmol/l)	336 ± 39	2,089 ± 370
Plasma ALT (U/L)	29.5 ± 1.9	959 ± 93
Plasma total CK-18 (ng/ml)	0.11 ± 0.02	4.9 ± 0.3
Liver triglycerides (mg/g tissue)	7.4 ± 0.7	55 ± 0.2
Liver hydroxyproline (µg/mg tissue)	0.03 ± 0.01	0.1 ± 0.01

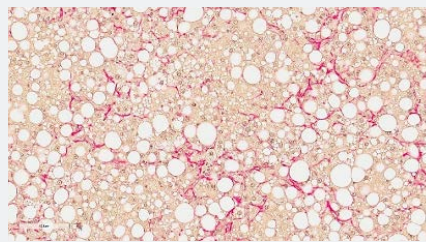
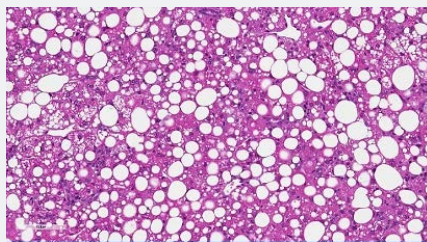


Clinical histopathological scores

Application of clinical-derived NAFLD Activity Score (NAS) and Fibrosis Stage (Kleiner, 2005). NAS is a composite score of steatosis, lobular inflammation and ballooning degeneration.

All features are assessed using our in-house developed deep learning based APP (GHOST - Gubra Histopathological Objective Scoring Technology).

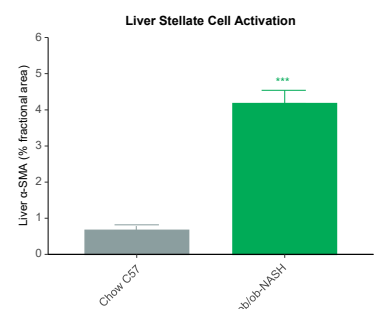
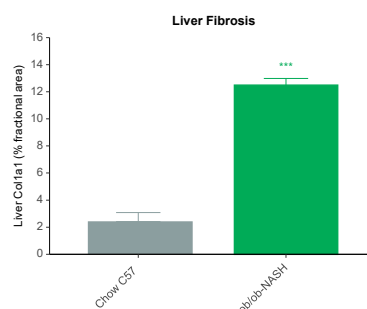
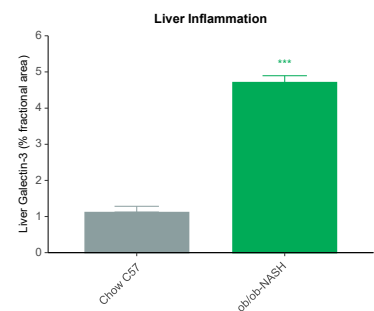
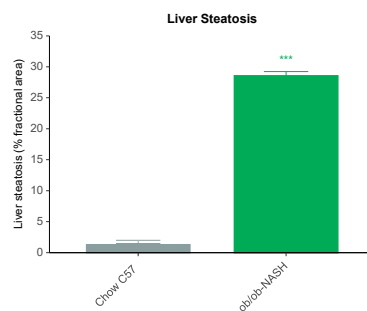
[Find more information on GHOST here.](#)



HE and PSR staining

Histomorphometric evaluation of steatohepatitis and fibrosis

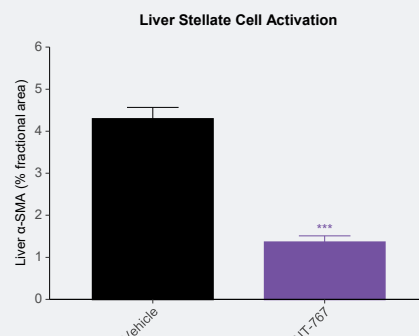
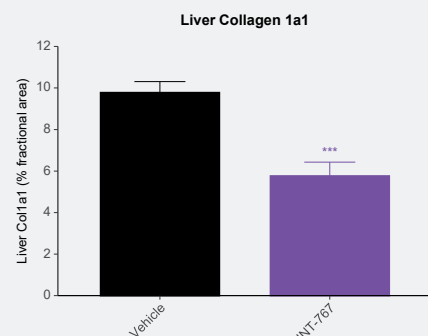
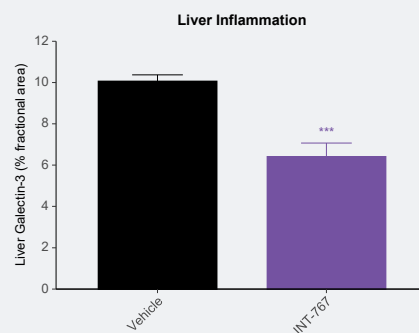
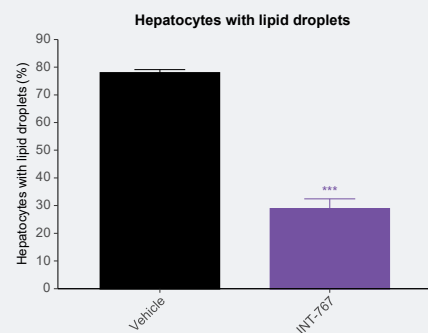
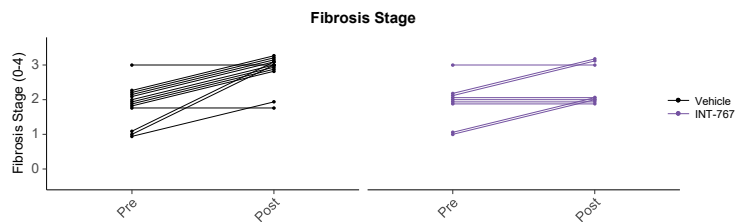
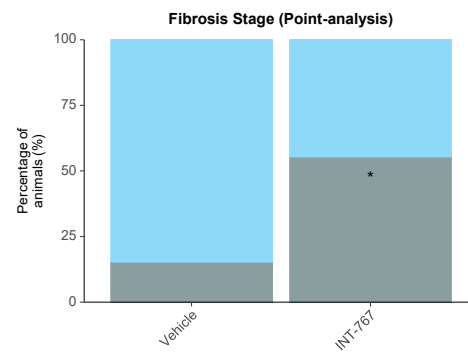
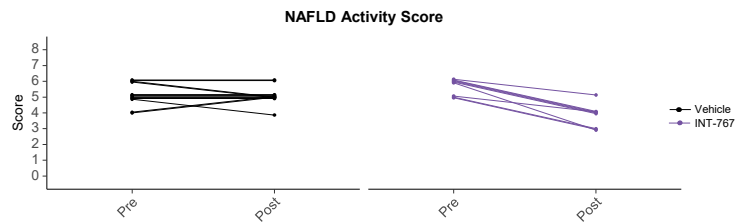
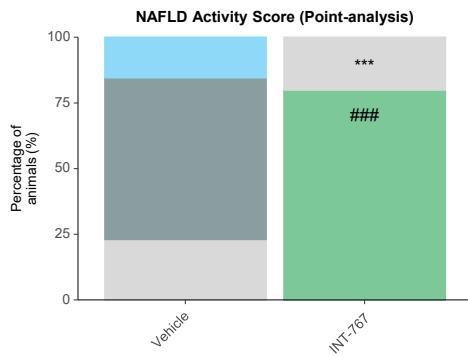
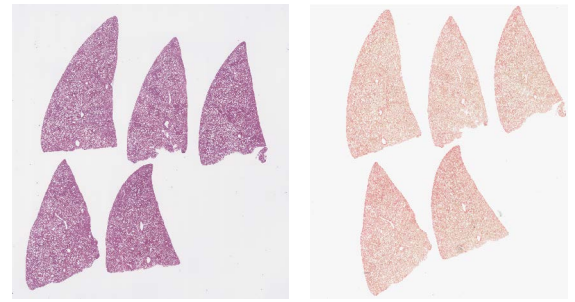
Terminal endpoints include quantitative assessment of steatosis, inflammation and fibrosis in addition to histopathological scoring (pre-to-post).



Individual pre-to-post NAFLD Activity Score and Fibrosis Stage

Assessment of pre-to-post NAFLD Activity Score and Fibrosis stage allows for evaluation of individual treatment effects on liver histopathology. Effect of 12 weeks of treatment with the FXR-TGR5 agonist INT-767.

HE (left) and PSR (right) stained biopsies.



Histomorphometric evaluation of steatohepatitis and fibrosis

Quantitative assessment of liver steatosis, inflammation and fibrosis by histomorphometric image analysis. Effect of 12 weeks of treatment with the FXR-TGR5 agonist INT-767.